

**REMARKS/ARGUMENTS:**

**Claim Amendments**

Claims 1-12, 14 and 16-18 are currently pending.

New claim 20 is presented. Support for new claim 20 can be found at least at page 3, line 26 - page 4, line 14 of the original specification. No new matter, nor new issues, are raised by new claim 20.

**Claim Rejections under 35 U.S.C. § 112, second paragraph**

1. The Examiner rejected Claim 12, 14 and 16-18 under 35 USC § 112, second paragraph, as being indefinite and grounds that the phrase "is derived from *Bacillus megaterium*" was unclear. More specifically, the Examiner asserts that it was unclear whether the monooxygenase "derived from *Bacillus megaterium*...comprising cytochrome P450 monooxygenase with an amino acid sequence comprising SEQ ID NO: 2 encompasses mutants of a single specific enzyme (SEQ ID NO: 2), or whether it encompasses mutants of any monooxygenase." The Examiner further asserted that, "[a]s applicants have not provided a definition for the above phrase, the Examiner has interpreted the claims broadly to mean that a monooxygenase derived from *Bacillus megaterium*...encompasses polypeptides which are recombinants, variants or mutants of any monooxygenase." Applicant respectfully traverses the rejection.

Upon review of the file history, it appears that the phrase "derived from" was added to the claims in response to the Examiner's use of such term in the Office Action of October 6, 2003. More specifically, the that Office Action, with regard to claims 14 and 15, the Examiner asserted that "the mutants of claims 14 and 15 have been interpreted as being derived from a *Bacillus megaterium* cytochrome P450 monooxygenase." Further, in Applicant's response such definition was clarified by reference to the specification. Accordingly, Applicant is perplexed as to how the Examiner can now assert that such phrase is and/or would be unclear to a skilled artisan. In this regard, it is apparent from the Examiner's use thereof that the scope and meaning of such phrase would have been sufficiently clear and understood by an ordinarily skilled artisan.

More particularly, the Examiner's use of such phrase serves as evidence and supports Applicant's contention that those having ordinary skill in the art regularly use such phrase and understand its meaning. In view thereof, the rejection should be withdrawn.

Additionally, Applicant submits that the Examiner has failed to consider the claim in its entirety. Further portions of Claim 12 recite:

...derived from *Bacillus megaterium* cytochrome P450 monooxygenase BM-3 with an amino acid sequence comprising SEQ ID NO:2 containing one functional mutation in each of amino acid sequence positions 87 and 188 and, optionally, at least one additional functional mutation in one of amino acid sequence positions 26, 47, 72, 74 and 354, wherein:

Phe 87 is replaced by Val, Ala or Leu;

Leu 188 is replaced by Asn, Gln, Arg, Lys, Ala, Gly, Ser or Trp;

Ala 74 is replaced by Val or Gly;

Arg 47 is replaced by His, Tyr or Phe;

Val 26 is replaced by Ser or Thr;

Ser 72 is replaced by Ala, Leu, Ile or Gly; or,

Met 354 is replaced by Ser or Thr,

Accordingly, it is respectfully submitted that the above excerpt of Claim 12 cannot reasonably be interpreted to encompass all polypeptides which are recombinants, variants or mutants of any monooxygenase as asserted by the Examiner. Rather, the claims must be read in light of the specification. In this regard, Applicant's specification, clearly defines "functional mutation." (P. 3 L.13-17). Therefore, the metes and bounds of the claim are sufficiently clear when read in light of the specification.

It is further submitted that new claim 20 does not include the phrase "derived from" in its claim language.

Accordingly, because the metes and bounds of claim 12 would be sufficiently clear to an ordinarily skilled artisan when read in light of the specification, withdrawal of the rejection is

courteously requested.

**Claim Rejections under 35 U.S.C. § 112, first paragraph**

1. The Examiner rejected claims 12, 14 and 16-18 under 35 USC § 112, first paragraph, as failing to comply with the written description requirement, i.e., that the claims contained subject matter that was not described in the specification in such a way as to reasonably convey to one having skill in the art that applicants had possession of the invention at the time of filing.

More specifically, the Examiner asserted, “the Examiner has interpreted the claims broadly to encompass a method of using a polynucleotide encoding mutants of any monooxygenase, including any monooxygenase isolated from any sources and including any or all variants, recombinants, and mutants thereof, comprising one or more amino acid mutation/substitution at amino acid positions corresponding to 87 and 188 and optionally at positions 26, 47, 72 and 354 of SEQ ID NO: 2 and one or more amino acid mutation/substitutions at any other amino acid positions. Therefore, the claims encompass a method for the production of subterminally hydroxylated aliphatic carboxylic acids using a polynucleotide encoding mutant monooxygenase having any structure...the specification only teaches a method for hydroxylating 15-paranitrophenoxycarboxylic acids (pNCA), 12-p-NCA, 10-pNCA or 8-pNCA with a polynucleotide encoding a mutant of a cytochrome p450 monooxygenase of SEQ ID NO: 2 wherein the mutant consists of mutations at positions 26, 47, 74, 87, 188 and/or 354 of SEQ. ID No: 2....given this lack of description of the representative species encompassed by the genus of claims, the specification fails to sufficiently describe the claimed invention in such full, clear, concise and exact terms that the skilled artisan would recognize that the applicants were in possession of the inventions of claims 12, 14 and 16-18.” Applicant respectfully traverse the rejection.

The Examiner’s contention that “during examination, the claims must be interpreted as broadly as their terms reasonably allow,” is improper. Indeed, “[d]uring patent examination, the pending claims must be “given their broadest reasonable interpretation consistent with the specification.”

*Phillips v. AWH Corp.*, 415 F.3d 1303, 75 USPQ2d 1321 (Fed. Cir. 2005). Additionally, “The broadest reasonable interpretation of the claims must also be consistent with the interpretation that those skilled in the art would reach.” *In re Cortright*, 165 F.3d 1353, 1359, 49 USPQ2d 1464, 1468 (Fed. Cir. 1999). Accordingly, the Examiner’s contention that “the claims encompass a method for the production of subterminally hydroxylated aliphatic carboxylic acids using a polynucleotide encoding mutant monooxygenase having *any* structure,” is not the broadest reasonable interpretation consistent with the specification. Claim 12 specifically recites that the vector includes a monooxygenase derived from SEQ ID NO: 2. The specification further describes that a monooxygenase derived from SEQ ID NO: 2 can include functional equivalents, which are described at pages 3-5 of the original specification. In view thereof, a skilled artisan would readily recognize that “derived from SEQ ID NO: 2,” did not describe “a polynucleotide encoding mutants of *any* monooxygenase, including *any* monooxygenase isolated from any sources and including any or all variants, recombinants, and mutants thereof,” as asserted by the Examiner, but would recognize that the claims were limited to a vector comprising SEQ ID NO: 2 and functional equivalents thereof. Thus, when properly construed by a skilled artisan, the specification provides sufficient description of the claimed invention to show that the inventors had possession of the invention at the time the application was filed.

Additionally, to satisfy the written description prong of 35 USC §112 ¶1, the specification need only describe the invention in sufficient detail such that one skilled in the art could clearly conclude that “the inventor invented the claimed invention” (*Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572 (Fed. Cir. 1997)). No particular form of disclosure is required, but “the description must clearly allow persons of ordinary skill in the art to recognize that [the patentee] invented what is claimed” (*In re Gosteli*, 872 F.2d 1008, 1012 (Fed. Cir. 1989)) (citing *In re Wertheim*, 541 F.2d 257, 262 (CCPA 1976)). “The analysis of whether the specification complies with the written description requirement requires the Examiner to compare the scope of the claim with the scope of the description to determine whether Applicant has demonstrated possession of the claimed invention. Such a review is conducted from the standpoint of one of skill in the art at the time the application was filed (see, e.g., *Wang Labs. v. Toshiba Corp.*, 993 F.2d 858, 865, 26 USPQ2d 1767, 1774 (Fed. Cir. 1993)) and should include a determination of the field of the invention and the level of skill and knowledge in the art.

Generally, there is an inverse correlation between the level of skill and knowledge in the art and the specificity of disclosure necessary to satisfy the written description requirement. Information which is well known in the art need not be described in detail in the specification. See, e.g., Hybritech, Inc. v. Monoclonal Antibodies, Inc., 802 F.2d 1367, 1379-80, 231 USPQ 81, 90 (Fed. Cir. 1986)(Emphasis added). “The ‘written description’ requirement must be applied in the context of the particular invention and the state of the knowledge.... As each field evolves, the balance also evolves between what is known and what is added by each inventive contribution.” Capon v. Eshhar, 418 F.3d 1349, 1357, 76 USPQ2d 1078, 1085 (Fed. Cir. 2005) (Emphasis added). If a skilled artisan would have understood the inventor to be in possession of the claimed invention at the time of filing, even if every nuance of the claims is not explicitly described in the specification, then the adequate description requirement is met. See, e.g., Vas-Cath, 935 F.2d at 1563, 19 USPQ2d at 1116; Martin v. Johnson, 454 F.2d 746, 751, 172 USPQ 391, 395 (CCPA 1972) (stating “the description need not be in *ipsis verbis* [i.e., “in the same words”] to be sufficient”).

Initially, as stated above, the Examiner has failed to account for certain claims terms, which are described in the specification and which affect how one of skill in the art would construe the claims. The instant claims refer to a functional mutation, which is specifically defined in the specification. Therefore, the Examiner cannot reasonably interpret the claims to contain all mutations, substitutions, at any amino acid position. A person of ordinary skill in the art would not interpret the claims to cover any monooxygenase having any structure. Further, those of ordinary skill in the art would readily recognize that enzymatic activity cannot be produced with “any structure” and therefore, the assumption that “any structure” is within the scope of the claims is not a reasonable interpretation.

Accordingly, because the Examiner’s has failed to apply a broadest reasonable interpretation of the claims that is consistent with the specification, and because the examples presented in Applicant’s specification sufficiently illustrate that Applicant was in possession of the invention, as broadly claimed, and/or that the inventors invented the claimed invention, Applicant respectfully submits that an ordinarily skilled artisan would recognize that Applicant was in possession of the claimed invention

In view thereof, the rejection should be withdrawn.

2. The Examiner rejected claims 12, 14 and 16-18 under 35 USC § 112, first paragraph, as not enabling a method “for the production of *any* subterminally hydroxylated aliphatic carboxylic acids using a polynucleotide encoding a mutant of *any* cytochrome p450 monooxygenase...[t]he specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims...the claims encompass a method for the production of *any* subterminally hydroxylated aliphatic carboxylic acids using a polynucleotide encoding mutant hydroxygenase having *any* structure...[t]he scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of p450 monooxygenase variants and mutants, broadly encompassed by the claims. [t]he claims encompass compounds with a widely varying structure and properties...it would require undue experimentation of the skilled artisan to make the claimed variants an mutants of *any* p450 monooxygenases and use the claimed variants and mutants of *any* p450 monooxygenase to produce *any* subterminally hydroxylated aliphatic carboxylic acids.” Applicant respectfully traverses the rejections.

As above, the Examiner bases the instant rejection on an improper construction of the phrase, “derived from *Bacillus megaterium*,” to incorrectly imply that the claims encompass, “*any* subterminally hydroxylated aliphatic carboxylic acids using a polynucleotide encoding a mutant of *any* cytochrome p450 monooxygenase.” As previously noted, a person having ordinary skill in the art would recognize that the claims were substantially limited to gene constructs/vectors/organisms, etc. comprising SEQ ID NO: 2 and functional equivalents thereof.

Additionally, it should be further appreciated that “[t]he specification need not explicitly teach those in the art to make and use the invention; the requirement is satisfied if, given what they already know, the specification teaches those in the art enough that they can make and use the invention without ‘undue experimentation’” (*Amgen Inc. v. Hoechst Marion Roussel, Inc.*, 314 F.3d 1313, 1334 (Fed. Cir. (2003))). As indicated above, the Examiner has failed to apply the broadest reasonable interpretation of the claims that is consistent with the specification. In

this regard, it is respectfully submitted that the Examiner has failed to properly assess the scope of the claims as written. The Examiner correctly states that “containing” is an open ended transition. However, Applicant respectfully submits that despite the fact that the claim is open-ended, the claimed mutant monooxygenase requires at least the specific mutations recited in the claims. When such limitations are combined with the fact that the skilled artisan would readily understand that the subterminally hydroxylated aliphatic carboxylic acid maintains its enzymatic activity, the mutant monooxygenase cannot comprise “any structure” as asserted by the Examiner. Further, an ordinarily skilled artisan will not start with “any P450 monooxygenases” when trying to produce a subterminally hydroxylated aliphatic carboxylic acid, rather, the skilled artisan would utilize starting products that lend themselves to the production of the particular products sought.

The Examiner admits that skilled artisans would be well apprised of well known isolation techniques, recombinant techniques and mutagenesis techniques. Further, there are well known routine screenings for multiple substitutions or multiple modifications are known. Accordingly, an ordinarily skilled artisan would apply such knowledge of such techniques in the context of the instant claims. Notwithstanding, the claimed monooxygenase comprises SEQ ID NO:2 along with specific functional mutations and the specification further sets forth examples and describes further functional mutations. Accordingly, given the descriptions and example set forth in the instant specification, coupled with that which is known by the ordinarily skilled artisan, it is clear that a skilled artisan would be quite capable of making and using the claimed invention.

Additionally, it should be further appreciated that that large amounts of experimentation are not necessarily considered undue if it is common or routine in the technical field to undertake such experimentation. For example, in the instant context, a skilled artisan would know that in certain positions, certain nucleic/amino acid modifications would render the subsequent protein inactive and would avoid using said substitutions. Additionally, computational techniques, available at the time the application was filed, would assist the skilled artisan in rendering protein structural predictions based on sequence listings. The Examiner is directed to, for example, the Boston University Protein Sequence Analysis server (available at [Page 14 of 16](http://bmerc-</a></p></div><div data-bbox=)

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www.bu.edu/psa/), which has been available since at least the filing date of the instant application, and which provides data for the skilled artisan searching for structural predictions based on amino acid sequences. Similarly, skilled artisans routinely search databases, such as GenBank, for homologous sequences in order to compare the known, to for example, the recently discovered. Consequently, the ordinarily skilled artisan would conduct such types of screening such that the any experimentation would not be undue. Accordingly, predicting function from sequence homology would have been an ordinary and routine activity for the skilled artisan.

In view thereof, reconsideration of the rejection is respectfully requested.



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**Conclusion**

Applicants respectfully submit that the present application is in condition for allowance, which action is courteously requested. Please charge any shortage in fees due in connection with the filing of this paper to Deposit Account 14.1437. Please credit any excess fees to such account.

Respectfully submitted,  
NOVAK DRUCE & QUIGG, LLP

A handwritten signature in black ink, appearing to read 'SPK' followed by a stylized flourish.

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